REMARKS

Amendments

Claims 1-79, 82-84 and 95-104 have been canceled, and claims 80, 81 and 85-91 have been amended. Upon entry of the amendment, claims 80, 81 and 85-94 will be pending. Support for the added claims can be found in the specification and in the claims as originally filed.

Rejections

Rejections under 35 U.S.C. § 101/112 1st paragraph

The Examiner has rejected claims 66-69, 71, 73 and 74 because the claimed invention is allegedly not supported by either a specific or substantial asserted utility or a well-established utility for the reasons of record.

The claims have been canceled rendering the rejection moot. Withdrawal is respectfully requested.

Rejections under 35 U.S.C. § 112, 1st paragraph

Claims 66 and 80 have been rejected for allegedly failing to satisfy the written description requirement.

The claims have been amended to delete reference to "allelic variants." Withdrawal is respectfully requested.

Rejections under 35 U.S.C. § 112, 1st paragraph

Claims 66-95 stand rejected for on the ground of lack of enablement.

The Examiner argues that phenotype is unpredictable, citing Moreadith and Sanford (it does not appear that a copy of Sanford was provided; Applicant reserves comment regarding this reference).

Applicant respectfully submits that the Examiner is confusing the issue of predicting *a priori* the phenotype of a knockout mouse with reproducibility (enablement) of the claimed invention. Moreadith is concerned with predicting phenotype where no previous knockout models exist, a clearly distinct situation . The Examiner has not cited any evidence that one skilled in the art would not be able to make or use the mouse having the phenotypes recited in

the specification. As recited in the claims and disclosed in the specification, the phenotypes are relative to a wild-type control mouse: i.e., a mouse of the same background as the transgenic mouse. If one skilled in the art desired to make the claimed invention in a background other than that described in the application, he/she would compare the knockout mouse with a control mouse of the same background.

Moreover, the Examiner has not cited any evidence suggesting that gross morphological changes, such as those phenotypes disclosed in the specification, are affected by background.

Additionally, the cited reference does not support the Examiner's broad statement that phenotype is unpredictable, or that phenotype does not correlate to function. According to Moreadith: "[t]his technology, which is typically used to create the null genotype ("knock-out" mice), has frequently provided the definitive experimental evidence regarding the functions of the encoded proteins." (page 208).

With regard to the heterozygous mouse (claim 80), the Examiner argues that the specification does not teach any phenotypes for the mice, and concludes therefore that the specification fails to teach one how to make and use such mice.

Applicant does not agree. The recitation of phenotypic differences is irrelevant to the issue regarding whether the specification enables the claimed mice. The specification clearly shows one how to make the heterozygous mice; and how to use such mice to create the homozygous mice (page 25, paragraph 1; Example 12).

Rejections under 35 U.S.C. § 112, 2nd paragraph

Claims 66-75 stand rejected as allegedly being indefinite. The claims have been canceled rendering the rejection moot. Withdrawal is respectfully requested.

Rejection under 35 U.S.C. § 102(a)

Claims 70, 72, 75, 77-79, 81 and 84 stand rejected as anticipated by Hodgson, which is cited as disclosing a mouse having a homozygous disruption in a target DNA sequence encoding a TRP.

Applicant respectfully disagrees. The "mouse" having a homozygous disruption in the HD gene was embryonic lethal – i.e., Hodgson does not disclose a mouse. Moreover, as amended, claim 80 recites a mouse whose genome comprises a disruption in a TRP gene, said

TRP gene encoding mRNA corresponding to the cDNA sequence of SEQ ID NO:47. Hodgson does not disclose a mouse (heterozygous or homozygous) having a disruption in the TRP gene, as defined. Therefore, the reference cannot anticipate the claimed invention. Withdrawal is respectfully requested.

Claims 70, 72, 75 and 77-79 stand rejected as anticipated by Lia, which is cited as disclosing cells having a homozygous disruption in a target DNA sequence encoding a TRP.

The claims have been amended rendering the rejection moot. Withdrawal of the rejection is respectfully requested.

In view of the above amendments and remarks, Applicant respectfully requests reconsideration and a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

The Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. **502775**.

Respectfully submitted,

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Date

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